

U.S.S.N. 09/665,303  
Filed: September 19, 2000  
AMENDMENT AND  
RESPONSE TO OFFICE ACTION

**Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

**Listing of Claims:**

1-56. (Canceled).

57. (Withdrawn) An implantable medical device for the controlled release of drug molecules comprising:

a substrate;  
at least two reservoirs in the substrate,  
release system disposed in the reservoirs, the release system comprising drug molecules for release; and  
discrete metal reservoir caps positioned over or within openings in the reservoirs, wherein release of the drug molecules from the device is activated by disintegration of the reservoir cap and the disintegration of the reservoir cap is actively controlled.

58. (Withdrawn) The device of claim 57, wherein the substrate is comprised of two or more substrate portions bonded together.

59. (Withdrawn) The device of claim 58, wherein the substrate comprises an upper substrate portion adjacent the reservoir cap and a lower substrate portion distal the reservoir cap.

60. (Withdrawn) The device of claim 59, wherein a reservoir section in the upper substrate portion is in communication with a reservoir section in the lower substrate portion, the two reservoir sections forming a single reservoir.

61. (Withdrawn) The device of claim 59, wherein the reservoir section in the lower substrate portion has a volume that is greater than the volume of the reservoir section in the upper substrate portion.

U.S.S.N. 09/665,303  
Filed: September 19, 2000  
AMENDMENT AND  
RESPONSE TO OFFICE ACTION

62. (Withdrawn) The device of claim 59, wherein the lower substrate portion is provided with an internal reservoir cap interposed between a reservoir section of the upper substrate portion and a reservoir section of the lower substrate portion, wherein release of the molecules from the reservoir section in the lower substrate portion is controlled by diffusion through or disintegration of the internal reservoir cap.

63. (Withdrawn) The device of claim 62, wherein the internal reservoir cap is disintegratable, so that the two reservoir sections become a single reservoir.

64. (Withdrawn) The device of claim 62, wherein the reservoir section of the lower substrate portion contains molecules different in quantity, type, or both quantity and type, from the molecules contained in the reservoir section of the upper substrate portion.

65. (Withdrawn) The device of claim 57, wherein disintegration of the reservoir cap is activated by direct application of electrical energy through the reservoir cap.

66. (Withdrawn) The device of claim 65, wherein at least one reservoir cap is an anode, and the device further comprises a cathode, a power source, and electrical circuitry means for application of an electric potential between the cathode and anode effective to disintegrate the reservoir cap.

67. (Withdrawn) The device of claim 57, wherein the release system further comprises at least one matrix material, excipient, or combination thereof.

68. (Withdrawn) The device of claim 57, wherein the release system further comprises at least one biodegradable or bioerodible polymeric material.

69. (Withdrawn) The device of claim 57, wherein the drug molecules comprise anesthetics, vaccines, chemotherapeutic agents, metabolites, immunomodulators, antioxidants, antibiotics, and ion channel regulators, or hormones.

U.S.S.N. 09/665,303  
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AMENDMENT AND  
RESPONSE TO OFFICE ACTION

70. (Withdrawn) The device of claim 57, wherein the disintegration of at least one of the reservoir caps is controlled by a signal from a biosensor or by a preprogrammed microprocessor.

71. (Withdrawn) A microchip device for the controlled release of drug molecules comprising:

a substrate;

at least two reservoirs in the substrate, wherein each reservoir has at least one opening defined in the substrate;

release system disposed in the reservoirs, the release system comprising drug molecules for release; and

at least two discrete electrically conductive reservoir caps, each reservoir cap closing off the opening defined by a respective reservoir,

wherein release of the drug molecules from the device is activated by disintegration of the reservoir cap by direct application of an electrical potential through the reservoir cap.

72. (Withdrawn) The device of claim 71, wherein the substrate is comprised of two or more substrate portions bonded together.

73. (Withdrawn) The device of claim 71, wherein at least one reservoir cap is an anode, and the device further comprises a cathode, a power source, and electrical circuitry means for application of an electric potential between the cathode and anode effective to disintegrate the reservoir cap.

74. (Withdrawn) The device of claim 71, wherein the release system in at least one of the reservoirs differs in quantity, type, or both quantity and type, from the release system in at least one other of the reservoirs.

75. (Withdrawn) The device of claim 71, wherein the release system further comprises at least one matrix material, excipient, or combination thereof.

U.S.S.N. 09/665,303  
Filed: September 19, 2000  
AMENDMENT AND  
RESPONSE TO OFFICE ACTION

76. (Withdrawn) The device of claim 71, wherein the release system further comprises at least one biodegradable or bioerodible polymeric material.

77. (Withdrawn) The device of claim 71, wherein the reservoir caps are formed of a metal film.

78. (Withdrawn) The device of claim 71, wherein the drug molecules comprise anesthetics, vaccines, chemotherapeutic agents, metabolites, immunomodulators, antioxidants, antibiotics, and ion channel regulators, or hormones.

79. (Currently Amended) An implantable medical device for the controlled release of drug molecules comprising:

a substrate;

at least two discrete reservoirs provided in spaced positions in the substrate; and

a release system disposed in the at least two reservoirs, the release system

including drug molecules dispersed in a matrix material,

wherein the medical device is implantable inside a patient and the rate of release of the drug molecules from the reservoir *in vivo* is controlled by the matrix material.

80. (Previously Presented) The device of claim 79, wherein the substrate is comprised of two or more substrate portions bonded together.

81. (Previously Presented) The device of claim 79, wherein the matrix material comprises one or more hydrogels or synthetic polymers.

82. (Withdrawn) The device of claim 79, wherein the matrix material is non-degradable.

83. (Withdrawn) The device of claim 82, wherein release of the drug molecules from the reservoir is controlled by *in vivo* diffusion of the drug molecules from the matrix material.

U.S.S.N. 09/665,303  
Filed: September 19, 2000  
AMENDMENT AND  
RESPONSE TO OFFICE ACTION

84. (Withdrawn) The device of claim 82, wherein the non-degradable matrix material comprises one or more synthetic polymers selected from the group consisting of poly(ethers), poly(acrylates), poly(methacrylates), poly(vinyl pyrrolidones), poly(vinyl acetates), poly(urethanes), celluloses, cellulose acetates, and poly(siloxanes).

85. (Previously Presented) The device of claim 79, wherein the drug molecules are heterogeneously dispersed within the reservoirs.

86. (Previously Presented) The device of claim 79, wherein the drug molecules comprise one or more therapeutic agents selected from the group consisting of anesthetics, chemotherapeutic agents, hormones, immunomodulators, ion channel regulators, and antibiotics.

87. (Previously Presented) The device of claim 79, wherein the dose of drug molecules in one of the reservoirs is different from the dose of drug molecules in another of the reservoirs.

88. (Previously Presented) The device of claim 79, wherein the kinetics of release of the drug molecules from one of the reservoirs is different from the kinetics of release of the drug molecules from another of the reservoirs.

89. (Withdrawn) The device of claim 79, wherein at least one of the reservoirs comprises two or more layers of the release system.

90. (Withdrawn) The device of claim 89, wherein a first drug is contained in a first layer of the two or more layers, and a second drug is contained in a second layer of the two or more layers.

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U.S.S.N. 09/665,303  
Filed: September 19, 2000  
AMENDMENT AND  
RESPONSE TO OFFICE ACTION

91. (Currently Amended) ~~The device of claim 79, further comprising~~ An implantable medical device for the controlled release of drug molecules comprising:

a substrate;

at least two discrete reservoirs provided in spaced positions in the substrate;

a release system disposed in the at least two reservoirs, the release system including drug molecules dispersed in a matrix material;

at least two discrete degradable reservoir caps covering the at least two reservoirs, wherein the rate of release of the drug molecules from the reservoir *in vivo* is controlled by the matrix material.

92. (Previously Presented) The device of claim 91, wherein one of the reservoir caps is formed of a first material and the other of the at least two reservoir caps is formed of a second material, wherein the first material has a different disintegration rate *in vivo* compared to the second material.

93. (Previously Presented) The device of claim 91, wherein one of the reservoir caps has a first thickness and the other of the at least two reservoir caps has a second, greater thickness.

94. (Previously Presented) The device of claim 91, wherein the reservoir caps comprises one or more synthetic polymers.

95. (Withdrawn) The device of claim 79, further comprising at least two discrete non-degradable reservoir caps covering the at least two reservoirs, which caps further control the kinetics of release of the drug molecules from the reservoirs.

96. (Withdrawn) The device of claim 95, wherein the reservoir caps comprises one or more synthetic polymers.

97. (Previously Presented) The device of claim 79, comprising at least two rows of the at least two reservoirs in an array in the device.

U.S.S.N. 09/665,303  
Filed: September 19, 2000  
AMENDMENT AND  
RESPONSE TO OFFICE ACTION

98. (Previously Presented) The device of claim 97, wherein a first release system is the reservoirs of a first row and a second release system is in the reservoirs of another of the at least two rows, the first release system releasing the one or more drugs at a rate or in a dosage amount different from release of the one or more drugs from the second release system.

99. (Currently Amended) ~~The device of claim 79 wherein the matrix material is, An~~  
implantable medical device for the controlled release of drug molecules comprising:  
a substrate;  
at least two discrete reservoirs provided in spaced positions in the substrate;  
a release system disposed in the at least two reservoirs, the release system  
including drug molecules dispersed in a degradable matrix material;  
wherein the rate of release of the drug molecules from the reservoir *in vivo* is  
controlled by the matrix material.

100. (Previously Presented) The device of claim 99, wherein the release of the drug molecules from the reservoirs is controlled by the *in vivo* disintegration of the matrix material.

101. (Previously Presented) The device of claim 99, wherein the disintegration of the degradable matrix material is by dissolution, enzymatic hydrolysis, or erosion.

102. (Previously Presented) The device of claim 99, wherein the degradable matrix material comprises one or more synthetic polymers selected from the group consisting of poly(amides), poly(esters), poly(anhydrides), poly(orthoesters), poly(carbonates), copolymers thereof, and mixtures thereof.

103. (Previously Presented) The device of claim 99, wherein the degradable matrix material comprises one or more synthetic polymers selected from the group consisting of poly(lactic acids), poly(glycolic acids), poly(lactic-co-glycolic acids), poly(caprolactones), and mixtures thereof.

U.S.S.N. 09/665,303  
Filed: September 19, 2000  
AMENDMENT AND  
RESPONSE TO OFFICE ACTION

104. (Withdrawn) The device of claim 99, wherein the at least two reservoirs individually comprise at least two layers of a release system and at least one layer of a degradable or soluble material which does not comprise the one or more drugs.

105. (Previously Presented) The device of claim 99, wherein the release system further comprises one or more pharmaceutically acceptable carriers, excipients, or diluents.

106. (Previously Presented) The device of claim 79, wherein the substrate comprises a metal.

107. (Previously Presented) The device of claim 79, wherein the reservoirs are made by a microfabrication process.

108. (Currently Amended) A microchip device for the controlled release of molecules comprising:

a substrate;

an array of two or more spaced apart reservoirs in the substrate,

a release system disposed in the reservoirs, the release system comprising chemical molecules for release; and

discrete polymeric reservoir caps positioned over or within openings of said at least two reservoirs,

wherein the release of the molecules from each reservoir is passively controlled by ~~diffusion through~~ or disintegration of the reservoir cap.

109. (Previously Presented) The device of claim 108, wherein the chemical molecules comprise one or more drugs for *in vivo* release.

110. (Previously Presented) The device of claim 108, wherein the substrate is comprised of two or more substrate portions bonded together.

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